Amendments to the specification:

Page 23

Please replace the first complete paragraph with the following amended paragraph.

The present invention is based on the surprising finding that the NCAM Ig2 domain strongly stimulates the outgrowth of neurites from NCAM present cells. [Thus, it has been found that NCAM Ig2 is a ligand of the NCAM Ig1 domain.] Thus, it has been found that NCAM Ig2 is a ligand of the NCAM Ig1 domain. It has further been found that the NCAM Ig2 domain stimulates neurite outgrowth by activation of specific signal transduction pathways.

Page 23

Please replace the last complete paragraph with the following amended paragraph.

The inventors have also, by means of combinatorial chemistry, identified small peptides which stimulate neurite outgrowth. [Active peptides selected from a peptide library have been identified, and a putative motif comprising two or more basic amino acid residues has been identified.] Active peptides selected from a peptide library have been identified, and a putative motif comprising two or more basic amino acid residues has been identified. The peptides have been shown to stimulate the same specific signal transduction pathways as the NCAM Ig2 domain.

Page 24

Please replace the first paragraph with the following amended paragraph.

The results show that ligands of NCAM Ig1, either the NCAM Ig2 domain or small functional mimics hereof, which are capable of activating specific signalling pathways, can promote neurite

outgrowth and thereby be of benefit in regeneration and learning. Other functional mimics of the NCAM Ig2 domain, such as antibodies and non-peptide molecules may be beneficial in the same way. [Therefore, the present invention provides compounds and compositions which are or comprise small peptides, polypeptides, which are or comprise small peptides, polypeptides, antibodies and non-peptide molecules recognizing the NCAM Ig1 domain. When applied to tissue containing NCAM-expressing cells these compounds and compositions will promote NCAM function.] Therefore, the present invention provides compounds and compositions which are or comprise small peptides, polypeptides, which are or comprise small peptides, polypeptides, antibodies and non-peptide molecules recognizing the NCAM Ig1 domain. When applied to tissue containing NCAM-expressing cells these compounds and compositions will promote NCAM function. The compounds and the compositions can be applied to promote functions of the nervous system, the muscles and any other NCAM-expressing tissues, including various organs.

Page 45

Please replace the first two complete paragraphs with the following amended paragraphs.

[Very interesting peptides are those which correspond to a part of the NCAM Ig2 domain, are a mimic or fragment of the NCAM Ig2 domain.

The peptides may bind to the Ig2 binding site on the NCAM Igl domain or to a binding site different from the NCAM Ig2 binding site. It is believed that the ligands C3, D3 and D4 bind to a site different from the binding site of NCAM Ig2 or fragments thereof.]

Very interesting peptides are those which correspond to a part of the NCAM Ig2 domain, are a mimic or fragment of the NCAM Ig2 domain.

The peptides may bind to the Ig2 binding site on the NCAM Igl domain or to a binding site different from the NCAM Ig2 binding site. It is believed that the ligands C3, D3 and D4 bind to a site different from the binding site of NCAM Ig2 or fragments thereof.

Page 45

Please replace the third complete paragraph with the following amended paragraph.

[Of likewise particular interest in addition to ligands of the Igl domain, are ligands of the Ig2 domain including the ligands of that part of the Igl-Ig2 binding site which is constituted by the Ig2 domain.] Of likewise particular interest in addition to ligands of the Igl domain, are ligands of the Ig2 domain including the ligands of that part of the Igl-Ig2 binding site which is constituted by the Ig2 domain.

Page 45

Please replace the fourth complete paragraph with the following amended paragraph.

Other compounds which are interesting compounds for the purposes of the present invention are [non-peptide] non-peptide molecules mimicking the binding of the NCAM Igl, the NCAM Ig2 domain or the artificial ligands. Such other compounds may be selected from small organic compounds, sugars and lipids, as well as peptidomimetics, peptides and peptomers.
molecules mimicking the binding of the NCAM Ig1, the NCAM Ig2 domain or the artificial ligands. Such other compounds may be selected from small organic compounds, sugars and lipids, as well as peptidomimetics, peptides and peptomers.

Page 47

Please replace the first full paragraph with the following amended paragraph.

Accordingly, the present invention relates to the NCAM Ig1 domain, the NCAM Ig2 domain and a fragment or a mimic thereof for [use] use in the treatment of a normal, degenerated or damaged NCAM presenting cell. An example of a fragment of the Ig1 domain is the part of the NCAM Ig1 domain which is involved in the NCAM Ig1-Ig2 binding site. In particular, the invention relates to the NCAM Ig2 domain, a fragment or a mimic thereof for use in the treatment of normal, degenerated or damaged NCAM presenting cells, which treatment consists of stimulating outgrowth from and/or proliferation of the NCAM presenting cells.

Pages 47-48

Please replace the paragraph bridging pages 47-48 with the following amended paragraph.

[The treatment] The treatment may suitably be a treatment of diseases and conditions of the central and peripheral nervous system, of the muscles or of various organs such as treatment of diseases or conditions of the central and peripheral nervous system, such as postoperative nerve damage, traumatic nerve damage, impair myelination of nerve fibres, postischaemic, e.g. resulting from a stroke, Parkinson's disease, Alzheimer's disease, dementias such as multiinfarct dementia, sclerosis, nerve degeneration associated with diabetes mellitus, disorders affecting the circadian clock or neuro-muscular transmission, and schizophrenia, treatment of diseases of muscles including conditions with impaired function of neuro-muscular connections such as genetic or traumatic atrophic muscle disorders, a treatment of diseases of various organs, such as degenerative conditions of the gonads, of the pancreas such as diabetes mellitus type I and II, of the kidney such as nephrosis and of the heart, liver and bowel and treatment or stimulation of the ability to learn and/or of the memory.

Page 58

Replace the second complete paragraph with the following amended paragraph.

The following three mutations were made and the mutated NCAM (20-208) domains were produced as recombinant proteins: NCAM (20-208) with three mutations in the domain- 1 E30A, E35A, K37A, NCAM (20-208) with three mutations in the domain-2 R192A, R196A, E198A and NCAM (20-208) with three mutations in the domain-1 E30A, E35A, K37A and three mutations in the domain-2 R192A, R196A, E198A. Mutations in the two sites of interest were introduced by PCR using 75 bp long 5' and 72 bp long 3' primers containing the mutations (5' CTG CAG GTA GAT ATT GTT CCC AGC CAA GGA GCC ATC AGC GTT GGA GCC TCC GCC TTC TTC CTG TGT CAA GTG GCA 3' (SEQ ID NO: 49) and 5'ATT CAC AAT GAC CTG AAT GTC CTT GAA GTT GAT GGC CCC GGC GGC CAG GAT GGC GCC CTC ACA GCG GTA AGT 3' (SEQ ID NO: 50)).

Page 61

Please replace the first complete paragraph, which immediately follows the heading "Synthesis of peptides", with the following amended paragraph.

One peptide, Igl-p [(SEQ ID NO: 26)] (SEQ ID NO: 26) derived from the sequence of NCAM Ig1 was synthesised as described below. In addition, one peptide, Ig2-p (SEQ ID NO: 23) derived from the sequence of NCAM Ig2 was synethsised as described below. From combinatorial libraries 22 NCAM Ig1-binding sequences [(SEQ ID No: 1-22)] (SEQ ID No: 1-22) were identified.

Pages 61-62

Please replace the paragraph bridging pages 61-62 with the following amended paragraph.

Three peptides, C3 [(SEQ ID NO:1), D3 (SEQ ID NO: 2)] (SEQ ID NO:1), D3 (SEQ ID NO: 2) and D4 (SEQ ID NO: 3) were selected for further analysis and synthesised on TentaGel resin with Rink amide linker (p-((R,S)-α-(1-(9H-fluoren-9-yl)-methoxyformamido)-2,4-dimethoxybenzyl)-

phenoxyacetic acid (Novabiochem)) using Fmoc-protected amino acids (3 eq.). Coupling was performed for >60 min. with TBTU (3 eq.), HOBt (3 eq.) And DIEA (4.5 eq.) in a manual multicolumn apparatus. Fmoc was deprotected with 20% piperidine in DMF for 10 min. Synthesis of peptide dendrimers was accomplished by coupling Fmoc-Lys (Fmoc)-OH (Novabiochem) to the linker resin followed by Fmoc-deprotection of the Fmoc group and further coupling of Fmoc-Lys (Fmoc)-OH was performed. After Fmoc-deprotection the synthesis of peptides was performed as above for the monomeric peptides. Peptidyl resins were deprotected with TFA 90%, 5% H_2O, 3% EDT, 2% thioanisole, precipitated in diethyl ether, washed three times in diethyl ether, solubilised in 5% AcOH and lyophilised. Amino acid analysis was performed using Waters picotag and Waters 501 pump connected to WISP 712. Waters 600E equipped with Waters 996 photodiode array detector was used for analytical and preparative HPLC on C_{18} columns (Delta-Pak 100Å 15µm, Millipore). MALDI-MS was done on a VG TOF Spec E, Fisions Instrument. The peptides were at least 95% pure as estimated by HPLC.